[0016] In one aspect, said mitigating agent is a monoclonal antibody. In another aspect, said method comprises using two, three, four or more mitigating agents.

[0017] In one aspect, a binding of said therapeutic protein to said target is measured by measuring receptor phosphorylation, phosphorylation of downstream proteins in a signal transduction pathway, cytokine release, cell proliferation, cell death, or production of a secondary protein. In another aspect, a binding of said therapeutic protein to said target is measured by the expression of a reporter gene. In a specific aspect, said reporter gene is luciferase.

[0018] In one aspect, said method further comprises a pre-treatment step of contacting said sample to said mitigating agent prior to contacting said sample to said therapeutic protein or said target.

[0019] This disclosure also provides a kit for carrying out the method of the invention. In some exemplary embodiments, the kit comprises a therapeutic protein, a target of said therapeutic protein, a neutralizing agent against said therapeutic protein, a competing drug, and a mitigating agent.

[0020] In one aspect, said kit further comprises cells that express said target. In a specific aspect, said kit further comprises cells that produce a measurable activity or signal in response to the binding of said therapeutic protein to said target. In another specific aspect, said activity is the expression of luciferase.

[0021] In one aspect, said target is immobilized to a solid support. In another aspect, said kit further comprises a label affixed to said therapeutic protein. In a specific aspect, said label comprises ruthenium.

[0022] These, and other, aspects of the invention will be better appreciated and understood when considered in conjunction with the following description and accompanying drawings. The following description, while indicating various embodiments and numerous specific details thereof, is given by way of illustration and not of limitation. Many substitutions, modifications, additions, or rearrangements may be made within the scope of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] FIG. **1**A shows a diagram of a cell-based neutralizing antibody (NAb) assay according to an exemplary embodiment. FIG. **1**B shows an increase in luciferase activity with increasing concentrations of a bispecific CD20×CD3 drug antibody, while a negative control antibody induces no luciferase signal according to an exemplary embodiment. FIG. **1**C shows an increase in luciferase activity with increasing concentrations of two bispecific BCMA×CD3 drug antibodies according to an exemplary embodiment.

[0024] FIG. **2**A shows a diagram of a cell-based NAb assay with the addition of neutralizing antibodies against each arm of a therapeutic antibody according to an exemplary embodiment. FIG. **2**B shows a decrease in luciferase activity with increasing concentrations of surrogate neutralizing antibodies against either the CD20 arm or the CD3 arm of a bispecific CD20×CD3 drug antibody according to an exemplary embodiment.

[0025] FIG. **2**C shows a decrease in luciferase activity with increasing concentrations of surrogate neutralizing antibodies against the BCMA arm of a bispecific BCMA×CD3 drug antibody according to an exemplary embodiment. FIG. **2**D shows a decrease in luciferase activity with increasing concentrations of surrogate neutralizing antibodies against the CD3 arm of a bispecific BCMA×CD3 drug antibody according to an exemplary embodiment. FIG. **2**E shows no change in luciferase activity with the addition of isotype control antibodies to a NAb assay for a bispecific BCMA×CD3 drug antibody according to an exemplary embodiment.

[0026] FIG. **2**F shows a decrease in luciferase activity with increasing concentrations of surrogate neutralizing antibodies against the BCMA arm of a second bispecific BCMA×CD3 drug antibody according to an exemplary embodiment. FIG. **2**G shows a decrease in luciferase activity with increasing concentrations of surrogate neutralizing antibodies against the CD3 arm of a second bispecific BCMA×CD3 drug antibody according to an exemplary embodiment. FIG. **2**H shows no change in luciferase activity with the addition of isotype control antibodies to a NAb assay for a second bispecific BCMA×CD3 drug antibody according to an exemplary embodiment.

[0027] FIG. **3**A shows a decrease in luciferase activity in a NAb assay for a bispecific CD20×CD3 drug antibody with the addition of competing antibodies against the drug target CD20 according to an exemplary embodiment. FIG. **3**B shows a decrease in luciferase activity in a NAb assay for a bispecific CD20×CD3 drug antibody with the addition of competing antibodies against the drug target CD3 according to an exemplary embodiment. FIG. **3**C and FIG. **3**D show a decrease in luciferase activity in a NAb assay for a bispecific BCMA×CD3 drug antibody with the addition of competing antibodies against the drug targets BCMA or CD3 according to an exemplary embodiment. FIG. **3**E and FIG. **3**F show a decrease in luciferase activity in a NAb assay for a second bispecific BCMA×CD3 drug antibody with the addition of competing antibodies against the drug targets BCMA or CD3 according to an exemplary embodiment.

[0028] FIG. **4**A shows an increase in luciferase activity in a NAb assay with increasing concentrations of therapeutic antibody according to an exemplary embodiment. The addition of naïve human serum had no effect on luciferase activity. FIG. **4**B illustrates the quantification of NAb assay signal by comparing luciferase activity in the presence of drug control to luciferase activity in the presence of experimental sample according to an exemplary embodiment.

[0029] FIG. **5** shows cell-based NAb assay results from 60 drug-naïve clinical samples according to an exemplary embodiment.

[0030] FIG. **6** shows a correlation between concentration of rituximab in clinical samples and NAb assay signal according to an exemplary embodiment.

[0031] FIG. **7**A shows a diagram of a cell-based NAb assay with the addition of rituximab according to an exemplary embodiment. FIG. **7**B shows a diagram of the NAb assay with the addition of rituximab and mitigating antibodies against rituximab according to an exemplary embodiment. FIG. **7**C shows the restoration of luciferase activity in the NAb assay with the addition of mitigating antibodies against rituximab according to an exemplary embodiment.

[0032] FIG. **8** shows the reduction of false positive NAb assay signal in drug-naïve clinical samples with the addition of mitigating antibodies against rituximab according to an exemplary embodiment.

[0033] FIG. **9**A shows a diagram of a target-capture ligand binding NAb assay according to an exemplary embodiment. FIG. **9**B shows a diagram of the target-capture ligand